Functional genomics approach to understanding sepsis heterogeneity

Le, Kieu

DOI:
10.33612/diss.98318779

Propositions

1. Heterogeneous endothelial responses may partially explain organ-specific failure phenotypes in sepsis (chapter 1).
2. Identifying specific genes and pathways affected by sepsis-associated loci is crucial to better understand the molecular mechanisms underlying sepsis heterogeneity (chapter 2).
3. The distinct genetic contribution to inflammatory responses associated with Candida infection, susceptibility to Candidaemia and patient outcome suggests multiple pathways and cell types play a role in sepsis pathogenesis (chapter 3).
4. Endothelial cells do not recognize pathogens directly, but rather actively regulate inflammation by responding to immune-cell-secreted humoral signals (chapter 4).
5. Modulating the activity of the Interferon (alpha, beta and gamma) and TNF pathways should be tested in a preclinical model for sepsis and a subgroup of sepsis patients (chapter 4).
6. To validate the role of a gene or pathway in sepsis, in vitro research should not focus on only one specific cell type, but rather on the interaction between different cell types such as leukocytes and endothelial cells.
7. Recent advances in the field of organoid and organ-on-chip technologies will provide opportunities to study sepsis-induced organ dysfunction in a humanized model.
8. Studying sepsis-associated alterations in the metabolome and microbiome could provide new opportunities to rewrite sepsis outcomes.
9. Education in the future should also focus on building up compassion and the ability to reinvent oneself. -adapted from Dalai Lama and Yuval Noah Harari.
10. “Wasn’t it extraordinary to be in the world right now, wandering around in a wonderful adventure!”- Jostein Gaarder, Sophie’s world.